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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,344	07/14/2003	Gene Liau	4-31617B	8482

1095 7590 03/07/2006

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,344	LIAU ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1,15-22,29-32 and 40-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-14,23-28 and 33-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/03; 11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-42 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group 2 (claims 2-14, 23-28, 33-39) in the reply filed on 11/29/2005 is acknowledged.

Claims 1, 15-22, 29-32 and 40-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/29/2005.

1. Claims 2-14, 23-28 and 33-39 are examined herein.

Claim Objections

Claims 2-14 and 33-39 are objected to because they depend from claims 1, 15, 16, 17, 29-32 and 40-42, which encompass a method comprising administering sphingosine kinase to a subject. The term "sphingosine kinase" would be recognized by one of ordinary skill in the art to be sphingosine kinase protein. Therefore, claims 1, 15, 16, 17, 29-32 and 40-42 are interpreted as protein therapy. Claims 2-14, 23-28 and 33-39, encompass a method comprising administering a polynucleotide encoding sphingosine kinase, which is gene therapy. However, claims 2-14 and 33-39 but are dependent on claims which are drawn to a method comprising administering sphingosine kinase polypeptide to a subject. Methods of administering polypeptides (protein therapy) are unrelated and patentably distinct from methods of administering nucleic acid sequences which encode a polypeptide (gene therapy). Furthermore,

protein therapy methods do not encompass gene therapy methods. Therefore, claims 2-14 and 33-39 are improper dependent claims and applicants should consider re-writing the improper dependent claims such that they do not depend on protein therapy claims. In the interest of compact prosecution, the Examiner has interpreted claims 2-14 and 33-39 as if they were not improper dependent claims and the claims have been grouped accordingly. It is noted that claims 23-28 are not improper dependent claims.

Claim Rejections - 35 USC § 112, first paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2-14, 23-28 and 33-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass polynucleotide encoding a sphingosine kinase, analogue, fragment, or derivative thereof. Therefore, the instant claims encompass nucleic acid sequences which are different from those disclosed in the specific SEQ ID Nos: 1, 3 and 5, and includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the named SEQ ID Nos. Thus, applicant has express possession of only SEQ ID NO: 1, 3 and 5, in a genus which comprises hundreds of millions of different possibilities considering every possible analogue, fragment, or derivative.

The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common element or attributes of the sequences are disclosed. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations are provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that:

> "In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, not every variant or fragment is described, only certain specific SEQ ID NOS are described.

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which represent functional variants or fragments of nucleic acids which have the claimed function. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 2, 3, 5, 6, 23-26, 33, 34, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Spiegel et al. (WO 99/61581, published Dec. 2, 1999).

Spiegel teaches a viral vector comprising a polynucleotide encoding sphingosine kinase, analogue, fragment or derivative thereof; wherein the viral vector is an adenoviral vector (e.g. see abstract; p. 23, lines 17-25; p. 9, lines 25-35; and Figures 1 and 2). Furthermore, Spiegel teaches that sphingosine kinase can be expressed in a subject by delivering a polynucleotide encoding a sphingosine kinase to the subject for the treatment or amelioration of a disease associated with sphingosine kinase (e.g., see page 6, lines 4-6; page 7, lines 25-35; page 8, lines 5-11. 20-26; page 38, lines 28-35; page 39).

6. Claims 2-5, 23-26 and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (US Patent 5,932,540).

It is noted that the claims encompass a viral vector comprising a polynucleotide encoding sphingosine kinase, analogue, fragment or derivative thereof, and a polynucleotide encoding VEGF. The claim encompasses any possible derivative or fragment of sphingosine kinase. Additionally, the claim encompasses any form of "VEGF" because the claims do not limit "VEGF" to any particular VEGF molecule. Therefore, the claim encompasses a viral vector comprising a polynucleotide encoding any VEGF and any other amino acid sequence, as any other possible amino acid sequence could be derived from sphingosine kinase.

Hu teaches a method comprising administering a viral vector comprising a polynucleotide encoding VEGF2 (see column 14, lines 4-10), and another sequence fused in frame with VEGF2 such that VEGF2 is expressed as a fusion protein to a subject in order to express the protein in the subject for the treatment/amelioration of a disorder. VEGF2 may be

expressed as a fusion protein with a leader sequence which functions as a secretory sequence for controlling transport of a polypeptide from the cell (see column 6, lines 60-67), a marker sequence which allows for purification of the polypeptide of the present invention (see column 7, lines 11-21), a compound to increase the half-life of the polypeptide (see column 11, lines 12-20), an N-terminal identification peptide imparting desired characteristics, or VEGF2 fused to a heterologous polypeptide (see Hu, claim 16). All of which can be derived from sphingosine kinase. For instance, Hu teaches the VEGF2 amino acid sequence in Figure 1. The sequence of Figure 1 comprises a polynucleotide encoding methionine (see the first amino acid of Figure 1). Therefore the sequence of Figure 1 teaches a viral vector including a polynucleotide encoding VEGF and comprising a polynucleotide encoding a fragment of sphingosine kinase, considering methionine is a fragment of sphingosine kinase (see first amino acid of Figure 1 of the instant application). Hu also teaches that the polynucleotide of Figure 1 comprises a polynucleotide encoding histidine (see the second amino acid of Figure 1). Therefore the sequence of Figure 1 teaches a viral vector including a polynucleotide encoding VEGF and comprising a polynucleotide encoding a fragment of sphingosine kinase, considering histidine is a fragment of sphingosine kinase (see amino acid number 59 of Figure 1 of the instant application). Therefore Hu anticipates the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 3, 6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiegel et al. (WO 99/61581).

As noted above, Spiegel teaches a viral vector comprising a polynucleotide encoding sphingosine kinase, analogue, fragment or derivative thereof; wherein the viral vector is an adenoviral vector (e.g. see abstract; p. 23, lines 17-25; p. 9, lines 25-35; and Figures 1 and 2). Furthermore, Spiegel teaches that sphingosine kinase can be expressed in a subject by delivering a polynucleotide encoding a sphingosine kinase to the subject for the treatment or amelioration of a disease associated with sphingosine kinase (e.g., see page 6, lines 4-6; page 7, lines 25-35; page 8, lines 5-11. 20-26; page 38, lines 28-35; page 39).

Spiegel does not teach the specific amount of the adenoviral vector which is administered to the subject.

It would have been prima facie obvious to perform routine optimization to identify the effective dosage of the vector. Applicants are reminded that MPEP 2144.05 II states,

> "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)."

Therefore, routine optimization is not considered inventive and no evidence has been presented that the selection specific concentration(s) of vector administered was other than routine or that the results should be considered unexpected in any way as compared to the closest prior art.

Claims 2, 3, 5, 7, 8, 11-14, 27, 28, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spiegel et al. (WO 99/61581) in view of U.S. Patent No. 6, 326,007 B1 (Yilma et al.).

As noted above, Spiegel teaches a viral vector comprising a polynucleotide encoding sphingosine kinase, analogue, fragment or derivative thereof; wherein the viral vector is an adenoviral vector (e.g. see abstract; p. 23, lines 17-25; p. 9, lines 25-35; and Figures 1 and 2). Furthermore, Spiegel teaches that sphingosine kinase can be expressed in a subject by delivering a polynucleotide encoding a sphingosine kinase to the subject for the treatment or amelioration of a disease associated with sphingosine kinase (e.g., see page 6, lines 4-6; page 7, lines 25-35; page 8, lines 5-11. 20-26; page 38, lines 28-35; page 39).

Spiegel does not teach that the viral vector is an lentiviral vector or that the vector is a BIV vector.

Yilma et al. teaches a lentiviral vector which is a bovine-immunodeficiency vector (BIV) which is useful for expressing a gene of interest, such as a therapeutic gene of interest, in a subject.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Spiegel and Yilma such that the viral vector used to express the sphingosine kinase polypeptide in the subject is the BIV vector (which is a lentiviral vector) with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by is based on the fact that adenoviral vectors and BIV (lentiviral vectors) are recognized in the art as equivalent vectors in that they can both be used to express a therapeutic protein in a subject. See MPEP 2144.06 and 2144.07 regarding the substitution of equivalents.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.E. Angell, Ph.D.
Art unit 1635

JON ANGELL
PATENT EXAMINER